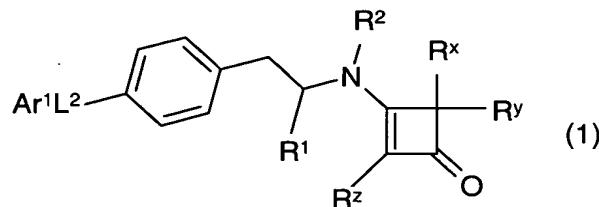


CLAIMS

1. A process for the preparation of a compound of formula (1):



5 wherein:

Ar¹ is an optionally substituted aromatic or heteroaromatic group;

L² is a linker group selected from -N(R⁴)- [where R⁴ is a hydrogen atom or an optionally substituted straight or branched C₁₋₆alkyl group], -CON(R⁴)- or -S(O)₂N(R⁴)-;

10 R¹ is a carboxylic acid (-CO₂H) or a derivative or biostere thereof;

R² is a hydrogen atom or a C₁₋₆alkyl group;

R^x, R^y and R^z which may be the same or different is each an atom or group - L¹(Alk¹)_n(R³)_v in which L¹ is a covalent bond or a linker atom or group, Alk¹ is an optionally substituted aliphatic or heteroaliphatic chain, R³ is a hydrogen or halogen atom or group selected from -OR^{3a} [where R^{3a} is a hydrogen atom or an optionally substituted straight or branched C₁₋₆alkyl group or C₃₋₈cycloalkyl group], -SR^{3a}, -CN or an optionally substituted cycloaliphatic, heterocycloaliphatic, polycycloaliphatic, heteropolycycloaliphatic, aromatic or heteroaromatic group, n is zero or the integer 1 and v is the integer 1, 2 or 3

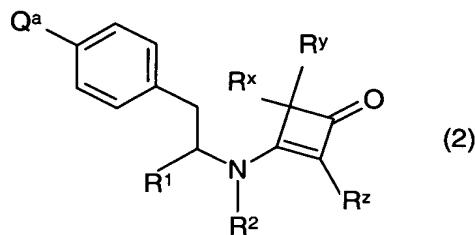
15 provided that when n is zero and L¹ is a covalent bond v is the integer 1;

20 or R^z is an atom or group as previously defined and R^x and R^y are joined together to form an optionally substituted spiro linked cycloaliphatic or heterocycloaliphatic group;

and the salts, solvates, hydrates and N-oxides thereof;

25

which comprises reacting a compound of formula (2):



wherein:

Q^a is a group $-\text{N}(\text{R}^4)\text{H}$;

and the salts, solvates, hydrates and N-oxides thereof;

5

with a compound Ar^1W wherein W is a group selected from X^1 (wherein X^1 is a leaving atom or group), $-\text{COX}^2$ (wherein X^2 is a halogen atom or a $-\text{OH}$ group) or $-\text{SO}_2\text{X}^3$ (in which X^3 is a halogen atom).

10 2. A process according to Claim 1 wherein the reaction is carried out in a solvent in the presence of an acid when W is the group X^1 .

3. A process according to Claim 2 wherein the solvent is selected from an alcohol, ether, acetic acid, water, acetonitrile, substituted amide or ester.

15

4. A process according to Claim 2 wherein the reaction is carried out in an alcohol in the presence of an acid catalyst.

20 5. A process according to Claim 1 wherein the reaction is carried out in the presence of a base, an organic amine or a cyclic amine and an organic solvent when W is the group COX^2 and X^2 is a halogen atom.

25 6. A process according to Claim 5 wherein the organic solvent is selected from a halogenated hydrocarbon, a dipolar aprotic solvent, an ether or an ester.

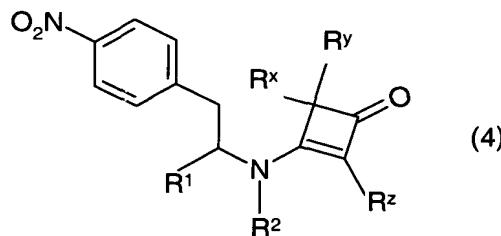
7. A process according to Claim 1 wherein the reaction is carried out in the presence of a condensing agent and a halogenated hydrocarbon, dipolar aprotic or an ether solvent when W is the group CO_2H .

30

8. A process according to Claim 1 wherein the reaction is carried out in the presence of a base, an organic amine or a cyclic amine and a halogenated hydrocarbon, dipolar aprotic or an ether solvent when W is the group SO_2X^3 .

5

9. A process according to any one of Claims 1 – 8 wherein the compound of formula (2) is prepared by reduction of a compound of formula (4):



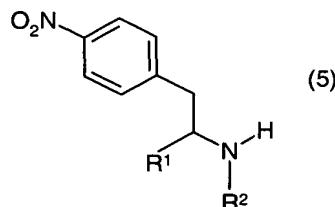
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10. A process according to Claim 9 wherein the reduction is carried out by catalytic hydrogenation or by chemical reduction.

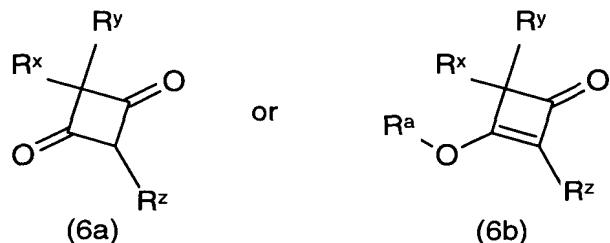
11. A process according to Claim 1 or Claim 9 wherein R^4 is a hydrogen atom.

15

12. A process according to Claim 9 wherein the compound of formula (4) is prepared by reaction of a compound of formula (5):



20 with a compound of formula (6a) or (6b):



wherein R^6 represents a C_{1-6} alkyl group or a silyl group.

13. A process according to Claim 12 wherein the reaction is carried out in the presence of an organic solvent.

5 14. A process according to Claim 13 wherein the solvent is selected from an aromatic hydrocarbon, a halogenated hydrocarbon or an ester.

15. A process according to any one of Claims 1 – 14 wherein R¹ is the group –CO₂Alk⁷.

10

16. A process according to any one of the preceding Claims which comprises subsequently interconverting a compound of formula (1) to another compound of formula (1).

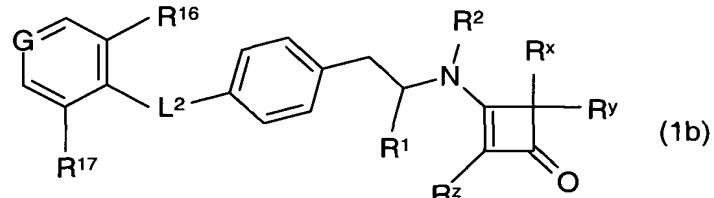
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17. A process according to Claim 16 which comprises hydrolysing a compound of formula (1) in which R¹ is –CO₂Alk⁷ to produce a compound of formula (1) in which R¹ is –CO₂H.

20

18. A process according to Claim 16 which comprises esterifying a compound of formula (1) in which R¹ is –CO₂H to produce a compound of formula (1) in which R¹ is –CO₂Alk⁷.

19. A process according to any one of the preceding Claims for the preparation of compounds of formula (1b):



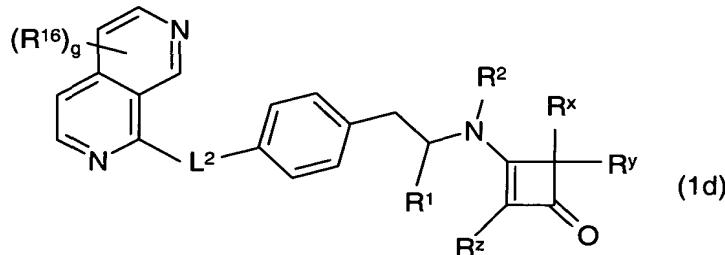
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wherein -G= is –CR¹⁸=, -N= or –N(O)=;

R¹⁶, R¹⁷ and R¹⁸, which may be the same or different is each a hydrogen atom or an atom or group -L³(Alk²)_tL⁴(R⁵)_u;
and the salts, solvates, hydrates and N-oxides thereof.

30

20. A process according to any one of the preceding Claims for the preparation of compounds of formula (1d):



wherein g is the integer 1, 2, 3 or 4;

5 R^{16} , is an atom or group $-L^3(Alk^2)_tL^4(R^5)_u$;
and the salts, solvates, hydrates and N-oxides thereof.

21. A process according to any one of the preceding Claims for the preparation of:

10 ethyl (2S)-2-[(2-bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate;
and the salts, solvates, hydrates and N-oxides thereof.

22. A process according to any one of the preceding Claims for the
15 preparation of:

ethyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-[4-([2,7]naphthyridin-1-ylamino)phenyl]propanoate;
and the salts, solvates, hydrates and N-oxides thereof.

20 23. A process according to any one of the preceding Claims for the preparation of:

ethyl (2*S*)-2-[(2-isopropylsulfanyl-3-oxo-7-oxa-spiro[3.5]non-1-en-1-yl)amino]-3-[4-([2,7]naphthyridin-1-ylamino)phenyl]propanoate; and the salts, solvates, hydrates and N-oxides thereof.

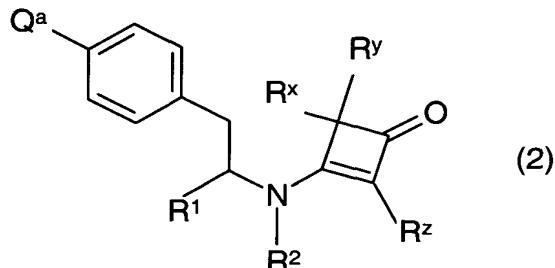
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24. A process according to any preceding one of the Claims for the preparation of:

2-hydroxyethyl (2*S*)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate;

and the salts, solvates, hydrates and N-oxides thereof.

25. A compound of formula (2):



5 wherein:

R^1 , R^2 , R^x , R^y and R^z are as defined in Claim 1;

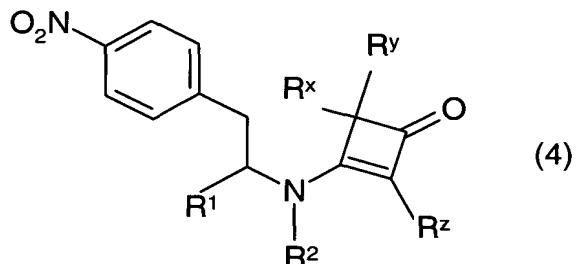
Q^a is a group $-N(R^4)H$;

and the salts, solvates, hydrates and N-oxides thereof.

10 26. A compound according to Claim 25 which is:

3-(4-aminophenyl)-2(S)-(3-oxo-7-oxaspiro[3.5]non-1-en-1-ylamino)-propionic acid hydroxyethyl ester.

27. A compound of formula (4):



15

wherein:

R^1 , R^2 , R^x , R^y and R^z are as defined in Claim 1;

and the salts, solvates, hydrates and N-oxides thereof.

20 28. A compound according to Claim 27 which is:

3-(4-nitrophenyl)-2(S)-(3-oxo-7-oxaspiro[3.5]non-1-en-1-ylamino)propionic acid hydroxyethyl ester.